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ASPIRIN-CONTAINING OINTMENT COMPOSITION FOR NEURALGIA TREATMENT
[Shinkeitsu chiryouyo asupiringanyu nankohzai soseibutsu]

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TITLE (54): ASPIRIN-CONTAINING OINTMENT COMPOSITION FOR NEURALGIA TREATMENT

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Specification

1. Title of the Invention

Aspirin-containing ointment composition for neuralgia treatment

2. Claims

(1) Aspirin-containing ointment composition for neuralgia treatment characterized by the fact that 0.5 to 5 wt% of aspirin (the effective constituent) and 0.5 to 30 wt% of aspirin solvent are blended in the ointment basis.

(2) Aspirin-containing ointment composition for neuralgia treatment characterized by the fact that 0.5 to 5 wt% of aspirin (the effective constituent), 0.5 to 30 wt% of aspirin solvent, and 20 wt% or less of absorption promoting agent are contained in the ointment basis.

3. Detailed Explanation of the Invention

(Industrial Field of Application)

This invention relates to an ointment composition for neuralgia treatment. In detail, this invention relates to an ointment composition which is superior in percutaneous absorbability and in its effect durability.

(Prior Art)

As an example of a neuralgia symptom, neuralgia occurring after belt-form herpes is explained.

Belt-form herpes is a viral infectious disease after chicken-pox-belt-form herpes, which is characterized by complications of eruptions

which are formed in a belt form and peripheral nerve disease. Said eruptions occur by forming small blisters along a certain sensory nerve control region. The nerve disease is mainly neuralgia, sometimes, though rarely, accompanied by motor nerve paralysis.

Said neuralgia appears most strongly after the occurrence of skin disease for several days, and subsides prior to the disappearance of the skin disease 7 to 10 days later. However, even after skin disease treatment, neuralgia symptoms may occur as sequela. This neuralgia may last for several years. Its frequency of occurrence is higher for older people. It has been reported that the frequency of occurrence is 1/3 for people 40 years old or older, and 100% for people 60 [legibility uncertain] years old or older.

As a method for the treatment of neuralgia which appears after belt-form herpes, a nerve block method, a medication method, an analgesic treatment by electric stimulation, or a freezing treatment are available. All of these methods, however, are not considered dependable. Since these methods, except for the medication method, cannot be practiced at home, the patient has to go to a hospital for treatment. Even with the medication method, the dependability of its effect is extremely insufficient when intractable neuralgia is treated by a medication method.

(Problems that the Invention is to Solve)

This invention intends to solve the aforementioned problems, and to propose an ointment composition for neuralgia treatment which can demonstrate an excellent analgesic effect even against intractable neuralgia because of its good percutaneous absorbability, and can also

demonstrate a long-lasting stable analgesic effect because of its effect's sustainability.

(Means of Solving the Problems)

The invented aspirin-containing ointment composition for neuralgia treatment is characterized by the fact that 0.5 to 5 wt% (in what follows, this is simply noted by %) of aspirin (the effective constituent) and 0.5 to 30% of aspirin solvent are blended in the ointment basis, and, as needed, 20% or less of absorption promoting agent can be added.

(Operation)

The constituents which constitute the invented ointment composition are explained below.

As an ointment basis, a mixture consisting of the solid constituent and the liquid constituent to be described below is generally used. Examples of solid constituents include hardened oils, vaseline, beeswax, lanolin, solid paraffin, stearic acid, glycerine monostearate, glycerine trimyristate, microcrystalline wax, cetyl alcohol, cetyl myristate, and various kinds of thermoplastic polymers (e.g., polyethylene resin and the like). Examples of liquid constituents include various kinds of mineral oils, diisopropyl adipate, liquid lanolin, liquid paraffin, diethyl sebacate, squalane, squalene, isopropyl palmitate, isopropyl myristate, hexyldecyl dimethyloctanoate, butyl stearate, octyldodecyl myristate, isopropyl myristate [sic], castor oil, glycerine tricaproate, and silicone oil. As an example of the most suitable ointment basis formed by blending these constituents, one formed by blending mineral oil and polyethylene resin can be mentioned (this is sold by Japan

Squibb Co. under the name of PLASTIBASE or HYDROPHILIC PLASTIBASE (trade name)). Furthermore, lanolin or vaseline itself can be satisfactorily used as an ointment basis without being blended with a liquid constituent.

Examples of aspirin solvent to be used in this invention include diethylene glycol monoethyl ether, ethylene glycol monomethyl ether, propylene carbonate, tributyl phosphate, trioctyl phosphate, ethyl lactate, N,N-dimethyl acetamide, crotamiton, ethylene glycol salicylate, and methyl ethyl ketone. Any one of these solvents or a mixture of at least two kinds of these solvents can be used.

In this invention, 0.5 to 5% of aspirin (relative to the total amount of ointment composition) is added in order to ascertain the treatment effect. Therefore, in order to ascertain the stability and durability of percutaneous absorption by uniformly distributing aspirin in the ointment basis, it is desired that at least 0.5% of aspirin solvent (relative to the total amount of ointment composition) be used; or preferably 1% or more of aspirin solvent be used. The upper limit of aspirin solvent addition, however, is 30%.

By such a constitution, the stability of the medicinal effect can be ascertained and the purpose of this invention can be achieved. However, in order to further improve the percutaneous absorbability, an absorption promoting agent can be added. Therefore, even though the quantity of an absorption promoting agent is small, the percutaneous absorbability can be proportionally improved. Thus, there is no special lower limit to the amount of its addition. However, a significant absorption promotion effect can be observed by an addition of at least

0.05% of an absorption promoting agent (or more preferably at least 0.1%). The recommended upper limit to the amount of addition of an absorption promoting agent is 50% (or preferably 30%). Examples of absorption promoting agent include oleic acid, sodium laurylsulfate, dimethylsulfoxide, dimethylformamide, N,N-dimethyl-m-toluamide, N,N-dimethyl-m-toluamide, polysorbate 40, 60, 65, 80, and the like. Any one of these ingredients or a mixture consisting of at least two kinds of these ingredients can be used.

It is sufficient to apply the invented ointment composition to the hypersensitively painful part for 1 to 4 times/day and 1 to 20 g/each time. The invented ointment composition can be used not only for treatment of neuralgia appearing after belt-form herpes, but also for treatment of various kinds of neuralgia symptoms including chronic arthritis.

(Working Examples)

Working Example 1

aspirin	2 (g)
dimethyl acetamide	2
N,N-dimethyl-m-toluamide	5
hardened rapeseed oil	30
glycerine monostearate	5
isopropyl myristate	56
	100

Working Example 2

aspirin	2 (g)
ethylene glycol salicylate	10

oleic acid	1	
hardened rapeseed oil	10	
stearic acid	30	
glycerine monostearate	5	
isopropyl myristate	32	
squalane	10	
	100	

Working Example 3

aspirin	2	(g)
dimethyl acetamide	2	
hardened rapeseed oil	30	
glycerine monostearate	5	
isopropyl myristate	61	
	100	

Working Example 4

aspirin	1	(g)
trioctyl phosphate	10	
sodium laurylsulfate	5	
vaseline	84	
	100	

Working Example 5

aspirin	2	(g)
methyl ethyl ketone	2	
solid paraffin	20	
polysorbate 80	5	
microcrystalline wax	10	
diisopropyl adipate	61	
	100	

Working Example 6

aspirin	1	(g)
propylene carbonate	3	
liquid paraffin	10	
plastibase	83	
polysorbate 40	2	
	100	

Working Example 7

aspirin	2	(g)
diethylene glycol monoethyl ether	4	
sodium laurylsulfate	2	
refined lanolin	25	
white vaseline	67	
	100	

Working Example 8

aspirin	2 (g)
tributyl phosphate	4
ethyl lactate	2
bleached beeswax	25
isopropyl palmitate	65
dimethylsulfoxide	2
	100

Working Example 9

aspirin	2 (g)
hardened rapeseed oil	35
crotamiton	2
glycerine monostearate	5
isopropyl myristate	56
	100

Working Example 10

aspirin	2 (g)
crotamiton	2
hardened rapeseed oil	7.5
glycerine monostearate	5
isopropyl myristate	69.5
stearic acid	14
	100

Comparative Example 1

aspirin	2 (g)
polysorbate 80	5
plastibase	93
	100

The ointment compositions shown in the Working Examples and Comparative Example were prepared based on the prescriptions shown above. Working Examples 1, 2, and 4 to 10 contain aspirin, ointment basis, aspirin solvent, and absorption promoting agent. Comparative Example 1, however, does not contain aspirin solvent; thus, this composition does not satisfy the condition required by this invention. Furthermore, Working Example 3 does not contain an absorption promoting agent. However, since the composition contains aspirin and aspirin solvent, this composition does satisfy the condition required by this invention.

Next, these ointment compositions were applied to 30 patients who were suffering from neuralgia appearing after belt-form herpes. In each application, 15 g of the ointment composition was applied to the hypersensitively painful part. Treatment results were evaluated according to five evaluation scales (i.e., very effective, effective, slightly effective, not effective, worsened). The results indicated that most of the ointments prepared in the Working Examples were either "very effective" or "effective." The ointment prepared in the Comparative Example was either "effective" or "slightly effective." With the ointments prepared in the Working Examples, an analgesic effect appeared within 3 to 5 minutes after the application, a complete analgesic effect was

realized within 10 minutes after the application, and the analgesic effect lasted for 5 to 7 hours.

When the ointments prepared in the Working Examples were applied to five patients who were suffering from chronic arthritis, either "very effective" or "effective" results were obtained.

Rat percutaneous permeation test

The ointment compositions prepared in Working Examples 1 and 3 and Comparative Example 1 were respectively applied to one side of the skin extracted from a rat's abdomen, and the applied side was contacted with the buffer solutions (pH: 6.8) having the following composition.

0.15 M	NaCl
0.47 mM	NaH_2PO_4
0.8 mM	NaH_2PO_4
22 ppm	gentamycin sulfate

Buffer solutions were sampled at 1, 2, 4, and 8 hours (20 μl in each sampling), and the amount of aspirin permeated into the buffer solution was quantitatively analyzed by HPLC.

Results are shown in Figure 1. The amount of aspirin permeated was in the order Working Example 1 > Working Example 3 >> Comparative Example 1.

(Effects of the Invention)

Since the invented ointment composition is constituted as described above, aspirin can be effectively percutaneously absorbed and its effect can last for a long period of time. In addition, simply by applying it to the affected part, an excellent analgesic effect can be realized instantly and can last for a long period of time.

4. Brief Explanation of the Figure

Figure 1 is graph showing the amount of aspirin permeation through rat skin.

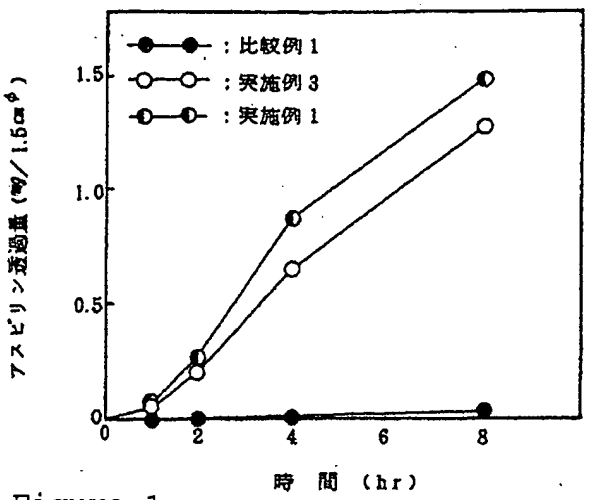

Figure 1
[vertical axis:] Amount of aspirin permeation (mg/1.5 cm^{ϕ})
[horizontal axis:] Time (hr)
[in graph, top to bottom:] Comparative Example 1
Working Example 3
Working Example 1